

This listing of claims will replace all prior versions, and listings, of claims in the application:

**LISTING OF CLAIMS:**

**Claims 1-89 (Canceled)**

**90. (Currently Amended)** A method of treating a disease, disorder or symptom associated with deficient endogenous levels of estrogen in women comprising orally administering to a woman having a deficient endogenous level of estrogen;

an estrogen in a sufficient amount to alleviate said disease, disorder or symptom, and micronized drospirenone in a sufficient amount to protect the endometrium from adverse effects of estrogen.

**91. (Previously presented)** A method according to claim 90, wherein the deficient levels of estrogen are caused by natural menopause, peri-menopause, post-menopause, hypogonadism, castration or primary ovarian failure.

**92. (Previously presented)** A method according to claim 90, wherein the disease, disorder or symptom is selected from the group consisting of hot flushes, sweating attacks, palpitations, sleep disorders, mood changes, nervousness, anxiety, poor memory, loss of confidence, loss of libido, poor concentration, diminished energy, diminished drive, irritability, urogenital atrophy, atrophy of the breasts, cardiovascular disease, changes in hair distribution, thickness of hair, changes in skin condition and osteoporosis.

93. **(Previously presented)** A method according to claim 92, wherein the disease, disorder or symptom is selected from the group consisting of hot flushes, sweating attacks, palpitations, sleep disorders, mood changes, nervousness, anxiety, urogenital atrophy, atrophy of the breasts and osteoporosis.

94. **(Previously presented)** A method according to claim 90, wherein the estrogen is selected from the group consisting of estradiol, estradiol sulfamates, estradiol valerate, estradiol benzoate, ethinyl estradiol, estrone, estriol, estriol succinate, conjugated estrogens and mixtures thereof.

95. **(Previously presented)** A method according to claim 94, wherein the estrogen is selected from the group consisting of estradiol, estradiol sulfamates, estradiol valerate, estradiol benzoate, estrone, and estrone sulfate and mixtures thereof.

96. **(Previously presented)** A method according to claim 95, wherein the estrogen is estradiol.

97. **(Canceled)**

98. **(Previously presented)** A method according to claim 90, wherein the estrogen is in micronized form.

**99. (Previously presented)** A method according to claim 96, wherein the estradiol is in micronized form.

**100. (Previously presented)** A method according to claim 90, wherein the dose of drospirenone corresponds to 15 to 70 mg per cycle.

**101. (Previously presented)** A method according to claim 90, wherein the amount of drospirenone corresponds to a daily dose ranging from 0.25 to 10 mg.

**102. (Previously presented)** A method according to claim 96, wherein the amount of estradiol corresponds to a daily dose ranging from 0.1 to 5 mg.

**103. (Previously presented)** A method according to claim 96 comprising administering estradiol in amounts corresponding to daily doses of 1 to 3 mg and drospirenone in amounts corresponding to daily doses of 1 to 3.5 mg.

**104. (Previously presented)** A method according to claim 96, comprising:  
a first treatment period of 10 to 12 days comprising administering a daily dosage unit comprising estradiol in an amount corresponding to a daily dose ranging from 0.1 to 5 mg;  
following the first treatment period, a second treatment period of 10 to 12 days comprising administering a daily dosage unit comprising estradiol in an amount corresponding to a daily dose of from 0.1 to 5 mg and drospirenone in an amount corresponding to a daily dose of from 0.25 to 6 mg; and

following the second treatment period, a third treatment period of 4 to 8 days comprising administering a daily dosage unit comprising estradiol in an amount corresponding to a daily dose of from 0.25 to 5 mg.

- 105. (Previously presented)** A method according to claim 96, comprising:
- a first treatment period of 10 to 12 days comprising administering a daily dosage unit comprising estradiol in an amount corresponding to a daily dose ranging from 0.1 to 5 mg;
- following the first treatment period, a second treatment period of 10 to 12 days comprising administering a daily dosage unit comprising estradiol in an amount corresponding to a daily dose of from 0.1 to 5 mg and drospirenone in an amount corresponding to a daily dose of from 0.25 to 6 mg; and
- following the second treatment period, a third treatment period of 4 to 8 days comprising administering a daily dosage unit of a placebo or blank.

- 106. (Previously presented)** A method according to claim 96, comprising:
- a first treatment period of at least 21 days comprising administering a daily dosage unit comprising estradiol an amount corresponding to a daily dose of from 0.1 to 5 mg and drospirenone in amount corresponding to a daily dose of from 0.25 to 6 mg; and
- following the first treatment period, a second treatment period of no more than 7 days comprising administering a daily dosage unit of a placebo or blank.

- 107. (Previously presented)** A method according to claim 96, comprising:  
a first treatment period of at least 21 days comprising administering a daily dosage unit comprising estradiol in an amount corresponding to a daily dose of from 0.1 to 5 mg and drospirenone in an amount corresponding to a daily dose of from 0.25 to 6 mg; and  
following the first treatment period, a second treatment period of no more than 7 days comprising administering a daily dosage unit comprising estradiol in an amount corresponding to a daily dose of from 0.1 to 5 mg.
- 108. (Previously presented)** A method according to claim 96, comprising administering for 21 to 28 days a daily dosage unit comprising estradiol in amounts corresponding to daily doses ranging from 0.1 to 5 mg and drospirenone in amounts corresponding to daily doses ranging from 0.25 to 6 mg.
- 109. (Previously presented)** A method according to claim 90, wherein the estrogen is administered continuously.
- 110. (Previously presented)** A method according to claim 90, wherein the estrogen and drospirenone are administered continuously.
- 111. (Previously presented)** A method according to claim 90, wherein the estrogen is administered continuously and drospirenone is administered sequentially.

**112. (Previously presented)** A method according to claim 111, wherein the estrogen dosage is lower for the first 1 to 7 days immediately after finalizing said sequential administration of drospirenone.

**113. (Previously presented)** A method according to claim 90, wherein estrogen is administered continuously and drospirenone is administered in an interrupted manner.

**114. (Previously presented)** A method according to claim 113, wherein estrogen is administered continuously for 21 to 30 days and drospirenone is administered in a 3-day-on-3-day-off cycle.

**115. (Previously presented)** A method according to claim 114, wherein drospirenone is administered on days 4 through 6, 10 through 12, 16 through 18, 22 through 24, and 28 through 30.

**116. (Previously presented)** A method according to claim 90, wherein the estrogen and the drospirenone are each administered sequentially with a treatment-free interval of 1-7 days within each cycle.

**117. (Previously presented)** A method according to claim 96, comprising:  
a first treatment period of administering for 20 to 24 days a daily dosage unit comprising estradiol in an amount corresponding to a daily dose of from 0.1 to 5 mg, and drospirenone in an amount corresponding to a daily dose of from 0.25 to 6 mg for the last 10 to 12 days of said 20 to 24 days, and

following the first treatment period, administering for 4 to 8 days a daily dosage unit comprising no active ingredient.

**118. (Previously presented)** A method according to claim 96, comprising:

a first treatment period of administering for 20 to 24 days a daily dosage unit comprising estradiol in an amount corresponding to a daily dose of from 0.1 to 5 mg, and drospirenone in an amount corresponding to a daily dose of from 0.25 to 6 mg for the last 10 to 12 days of said 20 to 24 days, and

following the first treatment period, administering for 4 to 8 days a daily dosage of unit comprising estradiol in an amount less than daily dosage unit taken for said 20 to 24 day administration of estradiol.

**119. (Previously presented)** A method according to claim 96, comprising:

a first treatment period of administering for 20 to 24 days a daily dosage unit comprising estradiol in an amount corresponding to a daily dose of from 0.1 to 5 mg, and drospirenone in an amount corresponding to a daily dose of from 0.25 to 6 mg for the last 10 to 12 days of said 20 to 24 days, and

following the first treatment period, not administering any dosage units for 4 to 8 days.

**120 - 121. (Canceled)**

**122. (Previously presented)** A method according to claim 108, wherein the daily dosage units are administered for 1 to 12 cycles of 28 days per cycle.

123. - 133. (Cancelled)

134. (Previously presented) The method according to claim 90, wherein the estrogen and/or the drospirenone is administered in the form of a tablet, capsule or pill.

135. - 136. (Cancelled)

137. (Previously presented) A method according to claim 90, wherein the estrogen is selected from the group consisting of estrone sulfate, 17 $\beta$ -estradiol sulfate, 17 $\alpha$ -estradiol sulfate, equilin sulfate, 17 $\beta$ -dihydroequilin sulfate, 17 $\alpha$ -dihydroequilin sulfate, equilenin sulfate, 17 $\beta$ -dihydroequilenin sulfate, 17 $\alpha$ -dihydroequilenin sulfate and mixtures thereof.

138. (Previously presented) A method for hormone replacement therapy comprising orally administering to a woman;  
a daily dose of 1 to 3 mg of an estrogen, and  
a daily dose of 0.25 to 10.0 mg of micronized drospirenone.

139. (Currently Amended) ~~A method for hormone replacement therapy comprising orally administering to a woman;~~

~~a daily dose of 1 to 3 mg of an estrogen, and~~  
~~a daily dose of 0.25 to 10.0 mg of drospirenone, A method of treating a disease, disorder or symptom associated with deficient endogenous levels of estrogen in women comprising orally administering to a woman having a deficient endogenous level of estrogen,~~

an estrogen in a sufficient amount to alleviate said disease, disorder or symptom,  
and drospirenone in a sufficient amount to protect the endometrium from adverse  
effects of estrogen,

wherein the drospirenone is in a form having a surface area of more than 10 000 cm<sup>3</sup>/g.

**140. (Currently Amended)** ~~A method for hormone replacement therapy comprising orally administering to a woman;~~

~~a daily dose of 1 to 3 mg of an estrogen, and~~

~~a daily dose of 0.25 to 10.0 mg of drospirenone, A method of treating a disease, disorder or symptom associated with deficient endogenous levels of estrogen in women comprising orally administering to a woman having a deficient endogenous level of estrogen,~~

an estrogen in a sufficient amount to alleviate said disease, disorder or symptom,

and drospirenone in a sufficient amount to protect the endometrium from adverse effects of estrogen,

wherein the drospirenone is in a form having a rapid dissolution such that at least 70% of said drospirenone is dissolved within 30 minutes from an oral dosage form of drospirenone when said dosage form is subjected to *in vitro* dissolution testing using USP XXIII Paddle Method operated with USP dissolution test apparatus 2, 900 ml of water at 37°C as dissolution medium and 50 rpm as the stirring rate.

**141. (Currently Amended)** A method of treating a disease, disorder or symptom associated with deficient endogenous levels of estrogen in women comprising orally administering to a woman having a deficient endogenous level of estrogen;

an estrogen in a sufficient amount to alleviate said disease, disorder or symptom, and micronized drospirenone in a sufficient amount to protect the endometrium from adverse effects of estrogen.

**142. (Previously presented)** A method according to claim 138, 139, 140 or 141, wherein the method is for treatment of deficient levels of estrogen caused by natural menopause, peri-menopause, post-menopause, hypogonadism, castration or primary ovarian failure.

**143. (Previously presented)** A method according to claim 138, 139, 140 or 141, wherein the estrogen is selected from the group consisting of estradiol, estradiol sulfamates, estradiol valerate, estradiol benzoate, ethinyl estradiol, estrone, estrone sulfate, estriol, estriol succinate, conjugated estrogens and mixtures thereof.

**144. (Previously presented)** A method according to claim 138, 139, 140 or 141, wherein the estrogen is in micronized form.

**145. (Previously presented)** A method according to claim 138, 139, 140 or 141, wherein the amount of drospirenone corresponds to a daily dose of 1 to 3.5 mg.

**146. (Previously presented)** A method according to claim 138, 139, 140 or 141, wherein the estrogen and drospirenone are administered continuously.

**147. (Previously presented)** A method according to claim 138, 139, 140 or 141, wherein the estrogen is administered continuously and drospirenone is administered sequentially.

**148. (Previously presented)** A method according to claim 147, wherein the estrogen dosage is lower for the first 1 to 7 days immediately after finalizing said sequential administration of drospirenone.

**149. (Previously presented)** A method according to claim 138, 139, 140 or 141, wherein estrogen is administered continuously and drospirenone is administered in an interrupted manner.

**150. (Previously presented)** A method according to claim 138, 139, 140 or 141, wherein estrogen is administered continuously for 21 to 30 days and drospirenone is administered in a 3-day-on-3-day-off cycle.

**151. (Previously presented)** A method according to claim 138, 139, 140 or 141, wherein the estrogen is ethinyl estradiol.

**152. (Previously presented)** A method according to claim 140, wherein at least 80% of said drospirenone is dissolved within 20 minutes by the stated test.

**153. (New)** A method according to claim 90, 138, 139, 140 or 141, wherein the drospirenone is in the form of a prodrug of the compound.

**154. (New)** A method according to claim 90, 138, 139, 140 or 141, wherein the drospirenone is provided in a daily dose of 0.25 to 8.0 mg and in a form whereby the drospirenone is exposed to the gastric environment upon dissolution.

**155. (New)** A method according to claim 90, 138, 139, 140 or 141, wherein the estrogen is sprayed from a solution onto particles of an inert carrier.

**156. (New)** A method according to claim 90, 138, 139, 140 or 141, wherein the estrogen is micronized such that 100% of the particles have a diameter of  $\leq 15.0 \mu\text{m}$ .

**157. (New)** A method according to claim 90, 138, 139, 140 or 141, wherein the estrogen is micronized such that 95% of the particles have a diameter of  $\leq 10.0 \mu\text{m}$ .

**158. (New)** A method according to claim 90, 138, 139, 140 or 141, wherein the estrogen is micronized such that 50% of the particles have a diameter of  $\leq 3.0 \mu\text{m}$ .

**159. (New)** A method according to claim 90, 138, 139, 140 or 141, wherein the estrogen and/or drospirenone are provided together with a carrier which promotes rapid dissolution of the estrogen and/or drospirenone.

**160. (New)** A method according to claim 90, 138, 139, 140 or 141, wherein the estrogen and/or drospirenone is provided together with a carrier which comprises carboxymethylcellulose, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, gelled starch, gelatin or polyvinylpyrrolidone.

**161. (New)** A method according to claim 90, 138, 139, 140 or 141, wherein the estrogen and/or drospirenone is provided together with a carrier which comprises polyvinylpyrrolidone.

**162. (New)** A method of hormone replacement therapy comprising administering to a woman in need thereof about 1 to about 3 mg of estradiol and about 1 to about 3.5 mg of drospirenone.

**163. (New)** A method of hormone replacement therapy comprising continuously administering to a woman in need thereof, in combined form, about 1 to about 3 mg of estradiol and about 1 to about 3.5 mg of drospirenone, said mg amounts being substantially constant during said administration.

**164. (New)** A method according to claim 90, 138, 139, 140, 141, 162 or 163 wherein the dose of estradiol is about 1 mg.

**165. (New)** A method according to claim 90, 138, 139, 140, 141, 162 or 163 wherein the dose of estradiol is about 1 mg and the dose of drospirenone is about 0.5 mg, about 1 mg, about 2 mg or about 3 mg.

**166. (New)** A method according to claim 90, 138, 139, 140, 141, 162 or 163 wherein the dose of drospirenone is from 0.25 to 6.0 mg.

**167. (New)** A method according to claim 90, 138, 139, 140, 141, 162 or 163 wherein the dose of drospirenone is from 0.5 to 4.5 mg.

**168. (New)** A method according to claim 90, 138, 139, 140, 141, 162 or 163 wherein the dose of drospirenone is from 1.5 to 3.5 mg.

**169. (New)** A method of claim 164 wherein the dose of estradiol is 1 mg.

**170. (New)** A method of claim 165 wherein the dose of drospirenone is 0.5 mg, 1 mg, 2 mg or 3 mg.

**171. (New)** A method of treating a disease, disorder or symptom associated with deficient endogenous levels of estrogen in women comprising orally administering to a woman having a deficient endogenous level of estrogen,

an estrogen in a sufficient amount to alleviate said disease, disorder or symptom,

and drospirenone in a sufficient amount to protect the endometrium from adverse effects of estrogen,

wherein the drospirenone is in a form having a rapid dissolution such that at least 70% of said drospirenone is dissolved from a tablet containing 3 mg of drospirenone in 900 ml of

water at 37°C within 30 minutes, as determined by USP XXIII Paddle Method using a USP dissolution test apparatus 2 and 50 rpm as the stirring rate.

**172. (New) A method of claim 140 wherein said oral dosage form is a tablet.**